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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte RAJIV SHAH and BAHAR REGHABI

Appeal 2009-011305
Application 10/715,143
Technology Center 1600

Decided: July 01, 2010

Before LORA M. GREEN, RICHARD M. LEBOVITZ, and
JEFFREY N. FREDMAN, Administrative *Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 by the Patent Applicant from the Patent Examiner's rejections of claims 1-17 and 19. The Board's jurisdiction for this appeal is under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF THE CASE

The claims in this appeal are drawn to a method of formulating a glucose oxidase (GO) enzyme comprising steps in which the “environment” of colonies of organisms with the enzyme is altered and then the colonies are screened “to identify colonies with active glucose oxidase after altering the environment of the colonies.”

Glucose oxidases are utilized in biosensors to detect glucose by catalyzing an enzyme reaction (Spec. 3: ¶ 6). Hydrogen peroxide is produced as a by-product of the reaction (*id.* at 3: ¶ 7). The peroxide molecule inactivates GO, limiting the biosensor’s lifetime (*id.* at 3: ¶¶ 7 & 8). To address this problem, a “directed evolution” technique is described by the inventors which utilizes genetic engineering techniques to produce enzymes with mutated sequences having improved peroxide-resistant properties (*id.* at 5: ¶¶ 13-15). To screen for the resistant enzymes, individual colonies with mutated GO are grown in culture and then the culture environment is altered, e.g., by addition of peroxide to the growth medium (*id.* at 6: ¶ 16). The GO enzyme is then tested for functionality to identify colonies with GO having the desired peroxide resistant properties.

Claims 1-17 and 19 are pending and stand rejected by the Examiner as follows:

1. Claims 1-3, 7-14, 17, and 19 under 35 U.S.C. § 103(a) as obvious in view of Valdes,¹ Cherry,² and Hatzinikolaou³ (Ans. 4);

¹ Valdes and Moussy. In Vitro and In Vivo Degradation of Glucose Oxidase Enzyme Used for an Implantable Glucose Biosensor. *Diabetes Technology & Therapeutics*, 2(3):367-376 (2000).

² Cherry et al. Directed evolution of a fungal peroxidase. *Nature Biotechnology*, 17: 379-384 (1999).

2. Claims 15 and 16 under 35 U.S.C. § 103(a) as obvious in view of Valdes, Cherry, Hatzinikolaou, and Misonix⁴ (Ans. 7); and

3. Claims 4-6 under 35 U.S.C. § 103(a) as obvious in view of Valdes, Cherry, Hatzinikolaou, Wagner,⁵ and Aldrich Catalog⁶ (Ans. 8).

Claim 1 is representative and reads as follows:

1. A method for formulating an enzyme comprising:
obtaining an organism with a glucose oxidase gene;
growing multiple colonies of the organism;
altering the environment of the colonies; and
screening the colonies to identify colonies with active glucose oxidase after altering the environment of the colonies.

This application is a divisional of Serial No. 10/035,918 (“the ‘918 application”), filed Dec. 28, 2001. The ‘918 application was the subject of Appeal 2009-011224 in which we affirmed the Examiner’s rejections (Decision (“Dec.”) decided March 22, 2010.). The rejections in the 2009-011224 appeal are the same as those in this appeal. Like the claims at issue in this appeal, the claims in the ‘918 application also had environment altering (“incubating the colonies in peroxide”) and screening steps to identify enzymes with glucose oxidase activity in the presence of peroxide. However, the ‘918 claims had additional steps of creating a library of

³ Hatzinikolaou et al. A new glucose oxidase from *Aspergillus niger*: characterization and regulation studies of enzyme and gene. *Applied Microbiology & Biotechnology*, 46: 371-381 (1996).

⁴ Misonix, *Ultrasonic Liquid Processors*, Cole Parmer Catalog, p. 2112.

⁵ EP 0 251 475 A1, Jan. 7, 1988.

⁶ Aldrich Catalog, 1998-1999, p. 1005.

mutated GO enzymes and inserting the mutated GO into host organisms prior to the altering and screening steps.

1. OBVIOUSNESS OVER VALDES, CHERRY,
& HATZINIKOLAOU

Findings of Fact

The findings (FF1-10) set forth in the Board Decision decided March 22, 2010 and in the Examiner's Answer (mailed March 9, 2009) are adopted in this decision.

Statement of the Issues & Discussion

The basis of the Examiner's rejection is the same in the instant appeal as it was in the appeal in the '918 application. In both appeals, the Examiner found that Valdes taught that GO was degraded by peroxide, but did not teach mutating GO to obtain mutants which were peroxide-resistant (Ans. 4-5). However, the Examiner found that Cherry described a genetic engineering method for producing enzymes resistant to hydrogen peroxide having the steps as recited in claim 1, with the difference that Cherry performed the method on a peroxidase enzyme, not glucose oxidase as claimed (Ans. 5-6). However, the Examiner found that Valdes had identified peroxide deactivation of GO as a problem associated with glucose sensor failure (*id.* at 4-5). The Examiner determined that persons of ordinary skill in the art would have had reason to apply Cherry's technique to Valdes' glucose oxidase enzyme to generate a mutant resistant to hydrogen peroxide, solving the problem articulated in the Valdes publication (*id.* at 6-7 & 12).

Appellants contend that the rejection is improper because:

There is no teaching or suggestion of the claimed invention because Valdes utilizes chemical additives to protect GO, taking a different direction than the mutagenesis method of the claimed invention (Appeal Br. 8-11 & 14-18);

Cherry has nothing to do with GO, but rather is related to production of a detergent additive that catalyzes dye oxidation (*id.* at 11); and

Hatzinikolaou's library of GO enzymes would have no purpose in Cherry's mutation process (*id.* at 12).

We have considered these arguments, but find they have been fully addressed in the Examiner's Answer and our previous decision in Appeal 2009-011224. Accordingly, we see no reason for further discussion, except to expand on following particular point:

As further evidence that the direction taken in the prior art is "wholly different from the [genetic engineering mutagenesis] direction of the present invention," Appellants cited the Yin and Heller references which described chemical and multi-layer structures to remove peroxide (Appeal Br. 15). Appellants contend that the "mass of evidence of record showing the direction of the industry (away from that of the present invention) cannot be ignored" (*id.* at 16).

This evidence is not persuasive. While it may be true that chemical and structural approaches had been used in the prior art to solve the GO peroxide problem, persons of ordinary skill in the art would not have been discouraged from taking other approaches, particularly when such approaches had been suggested by the prior art Cherry publication and shown to be successful (FF7-9). For a reference to "teach away" from using a particular approach, it must be shown that "the line of development

flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant." *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994). Appellants have not shown that persons of ordinary skill in the art would have doubted that Cherry's method would work when applied to GO. To the contrary, Cherry point to a number of examples in which relatively ineffective enzyme catalysts had been turned into commercially viable products by a variety of directed evolution techniques (FF8).

Appellants argument boils down to this: There is no evidence of record that mutagenesis had been used to make peroxide resistant GO. Rather, the prior art exclusively focused on chemical and structural approaches to protect the GO enzyme and therefore no one would have tried mutagenesis to achieve enzyme resistance.

In a section 103 rejection, there is difference between what was done in the prior art and what is claimed. However, section 103 bars patents on inventions that would have been obvious to persons of ordinary skill in the art. The burden is on the PTO is to establish why the ordinary skilled worker would have modified the prior art to have made what is claimed. In this case, the teaching by Cherry that mutagenesis is a valuable and operative method to produce enzyme resistance would have prompted the ordinary skilled worker to apply it to GO, even though this approach had not yet been used in the prior art.

On pages 21-22 of the Appeal Brief, Appellants contend that certain features of claim 1, 3, 7-14, and 17 distinguish them from the prior art. However, Appellants simply recited the features of the claims without explaining how the feature distinguished the claim over the prior art. "A

statement which merely points out what a claim recites will not be considered an argument for separate patentability of the claim.” 37 C.F.R. § 41.37(c)(1)(vii).

In sum, we affirm the rejection of claim 1. Claims 2, 3, 7-14, 17, and 19 fall with claim 1.

2. OBVIOUSNESS OVER VALDES, CHERRY, HATZINIKOLAOU, & MIXONIX

Statement of the Issue

Claim 15 depends indirectly on claim 1, and further recites that GO is removed from the colonies comprising “disrupting the colonies into cell components via sonication.” Claim 16, depends on claim 15, further reciting “wherein removing the glucose oxidase from the colonies further comprises fractionating the cell components employing centrifugation and differential solubility after disrupting the colonies via sonication.” To meet these limitations, the Examiner found that “the use of a sonicator, during protein purification is well known and routinely practiced in the art, see MISONIX” (Ans. 7). Misonix appears to be a list of different types of sonicators.

Appellants contend that the Misonix does not provide any motivation or suggestion to disrupt cells with glucose oxidase and that the Examiner did not address the limitations of claim 16 (Appeal Br. 16)

Legal Principles

An obviousness “analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in

the art would employ.” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007).

In assessing a claim’s obviousness, “a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions.” *Id.* at 417. “The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.” *Id.* at 416.

Discussion

In making an obviousness determination, the Examiner is not required to identify explicit teachings in the prior art that would have led persons of ordinary skill in the art to the claimed subject matter. *KSR*, 550 U.S. at 418. In this case, the Examiner found, as evidenced by Misonix, that sonicators were well known and routinely utilized in the prior art. Thus, the use of a sonicator to release GO from cells would have been the predictable use of prior art element according to its established function. *Id.*

While the Examiner did not explicitly point to a teaching of fractionating cells components as recited in claim 16, the Examiner concluded that these methods were conventional (Ans. 7) and therefore would have been a routine use of a known technique for its known function. The description of the purification steps in the Specification at page 13, paragraph 39, is consistent with the Examiner’s findings that Appellants have applied conventional protein purification techniques to the GO enzyme. An improvement which is a predictable use of a prior art element for its known purpose is obvious absent unexpected results or a showing of other secondary considerations. *KSR*, 550 U.S. at 416-418.

For the foregoing reasons, we affirm the rejection of claims 15 and 16.

3. OBVIOUSNESS OVER VALDES, CHERRY,
HATZINIKOLAOU, WAGNER, & ALDRICH CATALOG

Claims 4-6 are rejected over Valdes, Cherry, and Hatzinikolaou as for claim 1, and further in view Wagner and Aldrich Catalog. Appellants challenge the rejections only to the extent that Valdes, Cherry, and Hatzinikolaou do not each or suggested the steps recited in claim 1. As we have already found these arguments deficient for claim 1, we affirm the rejection of claim 4-6 or the reasons cited by the Examiner.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

Appeal 2009-011305
Application 10/715,143

dm

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